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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte
JOHN A. WOLFF, VLADAMIR S. TRUBETSKOY, AARON G. LOOMIS, PAUL M. SLATTUM, SEAN D. MONAHAN, JAMES E. HAGSTROM and VLADIMIR G. BUDKER

Appeal 2007-4262
Application 09/328,975
Technology Center 1600

Decided: December 21, 2007

Before TONI R. SCHEINER, DONALD E. ADAMS, and RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims 1, 3, 5, and 7. Of the remaining pending claims, the Examiner objected to claim 6 "for depending from a rejected claim and indicated that "[c]laim 8 is allowable" (Final Rej. 6). We have jurisdiction under 35 U.S.C. § 6(b).

INTRODUCTION

The claims are directed to a process for delivering a nucleic acid to a cell *in vivo*. Claim 1 is illustrative:

1. A process for delivering a nucleic acid to a cell *in vivo*, comprising:

a) forming a composition consisting of a nucleic acid associated via a non-covalent ionic interaction with a polycation in a solution wherein the composition has a net charge less negative than the nucleic acid;

b) ionically associating a polyanion with the composition of step a) in sufficient amount to form a complex having a net negative charge;

c) inserting the complex into a mammal;

d) delivering the complex to the cell.

The Examiner relies on the following prior art references to show unpatentability:

George Y. Wu et al., "Receptor-mediated Gene Delivery and Expression in Vivo," 263(29) *The Journal of Biological Chemistry*, 14621-14624 (1988).

Genevieve Degols et al., "Antiproliferative effects of antisense oligonucleotides directed to the RNA of *c-myc* oncogene," 19(4) *Nucleic Acids Research*, 945-948 (1991).

Carlo Leonetti et al., "Antitumor Effect of c-myc Antisense Phosphorothioate Oligodeoxynucleotides on Human Melanoma Cells In Vitro and in Mice," 88(7) *Journal of the National Cancer Institute*, 419-429 (1996).

Christopher M. Wiethoff et al., "The Potential Role of Proteoglycans in Cationic Lipid-Mediated Gene Delivery," 276(35) *The Journal of Biological Chemistry*, 32806-32813 (2001).

The rejections as presented by the Examiner are as follows:

1. Claims 1, 3, 5, and 7 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Degols, Leonetti, and Wiethoff.

2. Claims 1, 3, 5, and 7 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Wu and Degols.

We reverse rejection 1 and affirm rejection 2.

DISCUSSION

1. Claims 1, 3, 5, and 7 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Degols, Leonetti, and Wiethoff.

Claim 1 is reproduced above. Claim 1 requires, *inter alia*, that a composition be formed that consists of a nucleic acid and a polycation associated via a *non-covalent* ionic interaction. Claims 3, 5, and 7 depend from claim 1.

The Examiner relies on Degols to teach a composition comprising an anti-*c-myc* anti-sense oligonucleotide *conjugated* to polylysine, and then forming a ternary complex through the addition of polyanions, such as heparin (Answer 3). Thus, as Appellants point out, Degols "requires that the polycation be covalently linked to the nucleic acid" (Br. 8).

The Examiner relies on Wiethoff to support a conclusion that Degols' use of heparin will lead "to the formation of negatively charged ternary complexes" (Answer 4). The Examiner relies on Leonetti to teach "a method of delivering anti-*c-myc* anti-sense oligonucleotides to melanoma cells in mice" (Answer 5). However, neither Wiethoff nor Leonetti make up for Degols' failure to teach the association of a nucleic acid and a polycation through a *non-covalent* ionic interaction.

We are not persuaded by the Examiner's assertion that "the claims do not exclude the presence of a covalent linkage between the nucleic acid and the polycation, so long as there is also a noncovalent association between the two" (Answer 7). However, the Examiner provides no evidence that there is a noncovalent association between the anti-myc oligonucleotide and the polylysine. The Examiner appears to acknowledge the error in this argument by referring to the second rejection of record, which the Examiner states "is made against an embodiment of the claims as newly amended in which there is no covalent linkage between the polycation and the nucleic acid" (Answer 5).

Accordingly, we reverse the rejection of claims 1, 3, 5, and 7 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Degols, Leonetti, and Wiethoff.

2. Claims 1, 3, 5, and 7 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Wu and Degols.

The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Claim 1 is representative and is reproduced above.

The Examiner relies on Wu to teach a composition that consists of a nucleic acid and a polycation associated via a *non-covalent* ionic interaction (Answer 5). Specifically, the Examiner finds that Wu teaches the "formation of ionic complexes of polylysine and DNA and a method of delivering the complexes to cells in vivo" (*id.*). The Examiner recognizes, however, that Wu does "not teach formation of a complex having a net negative charge by ionically associating a polyanion with the

polylysine/DNA complexes" (*id.*). To make up for this deficiency, the Examiner relies on Degols to teach "that the toxicity of polylysine in delivery complexes can be reduced by formation of a ternary complex with an excess of polyanions such as heparin, carboxymethylcellulose, alginate, or polyglutamate" (Answer 6).

Based on this evidence the Examiner concludes that "[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to add a polyanion to the complex of Wu to form a negatively charged ternary complex prior to administration . . . to decrease the toxicity of the polylysine as taught by Degols" (*id.*). According to the Examiner, one would "reasonably expect addition of the polyanions to increase the stability of the complexes against nucleases, as well as to inhibit the maturation of endosomes to lysosomes after uptake of the DNA, thereby facilitating escape of the DNA from endosomes into the cytoplasm" (*id.*).

For their part, Appellants do not address Wu. Instead, Appellants focus attention on Degols, asserting that Degols requires the polycation to be covalently linked to nucleic acid in order to inhibit VSV (Br. 9). In further support of this argument, Appellants direct attention to Lemaitre[1] to teach that "no significant antiviral activity was observed when L929 cells were incubated with a mixture of poly(L-lysine) and 5' end sequence oligomers" (*id.*).

We are not persuaded by Appellants' argument. There is no requirement in claim 1 that the process be used to deliver a nucleic acid to a cell *in vivo* to treat viral infection generally, or VSV infection specifically. Thus, even if, as Appellants would argue, a covalent linkage of a polycation

[1] Lemaitre, 84 *Proc. Natl. Acad. Sci.* USA 648-652 (1987).

and nucleic acid is required for the composition to exhibit anti-viral activity, this argument bears little relationship to the scope of Appellants' claimed invention. In this regard, Wu expressly teaches the non-covalent association of a nucleic acid and a polycation for delivery of a nucleic acid to a cell *in vivo*. In the rejection before us on appeal, Degols is relied upon to teach the addition of "a polyanion to the complex of Wu to form a negatively charged ternary complex prior to administration . . . to decrease the toxicity of the polylysine as taught by Degols" (Answer 6). We find no error in the Examiner's prima facie case of obviousness. Appellants fail to address Wu, therefore Appellants have failed to establish an error in the Examiner's prima facie case of obviousness over the *combination* of Wu and Degols.

Accordingly, we affirm the rejection of claim 1 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Wu and Degols. Claims 3, 5, and 7 fall together with claim 1.

CONCLUSION

In summary, we reverse the rejection of claims 1, 3, 5, and 7 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Degols, Leonetti, and Wiethoff; and affirm the rejection of claims 1, 3, 5, and 7 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Wu and Degols.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

Ssc:

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